JACC Vol. 32, No. 4
October 1998:865–75

REVIEW ARTICLE

New Doppler Echocardiographic Applications for the Study of Diastolic Function

MARIO J. GARCIA, MD, FACC, JAMES D. THOMAS, MD, FACC, ALLAN L. KLEIN, MD, FACC

Cleveland, Ohio

Doppler echocardiography is one of the most useful clinical tools for the assessment of left ventricular (LV) diastolic function. Doppler indices of LV filling and pulmonary venous (PV) flow are used not only for diagnostic purposes but also for establishing prognosis and evaluating the effect of therapeutic interventions. The utility of these indices is limited, however, by the confounding effects of different physiologic variables such as LV relaxation, compliance and filling pressure. Since alterations in these variables result in changes in Doppler indices of opposite direction, it is often difficult to determine the status of a given variable when a specific Doppler filling pattern is observed. Recently, color M-mode and tissue Doppler have provided useful insights in the study of diastolic function. These new Doppler applications have been shown to provide an accurate estimate of LV relaxation and appear to be relatively insensitive to the effects of preload compensation. This review will focus on the complementary role of color M-mode and tissue Doppler echocardiography and traditional Doppler indices of LV filling and PV flow in the assessment of diastolic function.

(J Am Coll Cardiol 1998;32:865–75)

During the last two decades, Doppler echocardiography has emerged as the principal clinical tool for the assessment of left ventricular (LV) diastolic function. Echocardiography not only provides both anatomical and functional information but is also a widely available, safe and inexpensive imaging modality. Left ventricular filling and, more recently, pulmonary venous (PV) Doppler flow indices have been used to evaluate different parameters of diastolic function, including LV filling pressure, relaxation and stiffness (1–4). These indices are used not only for diagnostic purposes but also for establishing prognosis and evaluating the effect of therapeutic interventions (5–9). Unfortunately, since several physiologic variables affect simultaneously Doppler flow velocities, it is often difficult to determine which individual variables are affected when a specific Doppler pattern is observed unless other relevant clinical and/or invasive information is available (10–13). Recently, color M-mode and tissue Doppler have provided additional insights in the assessment of diastolic function. This review will focus on the complementary role of these new Doppler applications over the traditionally established pulsed Doppler flow indices.

From the Cardiovascular Imaging Center, Department of Cardiology, Cleveland Clinic Foundation, Cleveland, Ohio. Supported in part by Grant-in-aid #NEO-97-225-BGIA from the American Heart Association, North-East Ohio Affiliate (M.G.), National Aeronautics Space Administration Grant # NCC9-60, Houston, Texas (J.D.T., M.G.) and National Institute of Health Grant # ROI HL56688-01A1, Bethesda, Maryland (J.D.T.).

Manuscript received April 7, 1998; revised manuscript received June 9, 1998, accepted June 17, 1998.

Address for correspondence: Dr. Mario J. Garcia, Desk F-15, Division of Cardiology, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, Ohio 44195. E-mail: garciam@cesmtp.ccf.org.

Utility and Limitations of Standard Doppler Filling Indices

Transmitral Doppler velocities are related to transmitral pressure gradients as determined by Bernoulli's equation of flow (14,15). It must be realized that standard pulsed-wave Doppler velocities may be applied only to determine the convective component of the pressure gradient by using the simplified form of this equation. Doppler-derived pressure gradients are clinically accurate in diseased valves with restrictive orifices. However, in conditions of pulsatile flow across a nonrestrictive orifice such as a normal mitral valve, the relative contribution of the inertial component to the pressure gradient has been shown to be significant (16,17) and therefore true pressure gradients are underestimated.

Several clinical studies have shown an association between abnormalities of LV relaxation and specific transmitral Doppler flow velocity patterns. Patients with coronary artery disease, advanced age, hypertension and early restrictive cardiomyopathy typically exhibit a Doppler pattern of "delayed relaxation." This pattern, characterized by decreased early filling (E) and increased atrial contraction (A) mitral flow velocities, has been commonly attributed to a reduced LV relaxation rate (2,18–20). Impairment of LV relaxation results in prolongation of the isovolumic relaxation time (IVRT), decrease in early transmitral flow velocity (E) and prolongation of the E-wave deceleration time (15). However, other factors such as atrial and ventricular compliance, mitral valve inertance and left atrial (LA) pressure are also determinants of transmitral Doppler flow (11,13,15). Increasing filling pressure shortens isovolumic relaxation time, increases early transmitral gradient and transmitral flow velocity and reduces early flow decelera-

0735-1097/98/$19.00
PII S0735-1097(98)00345-3

Abbreviations and Acronyms

A_m	=	peak diastolic myocardial velocity during atrial contraction
AR	=	peak pulmonary venous atrial reversal velocity
D	=	peak diastolic pulmonary venous flow velocity
DT	=	early filling deceleration time
E	=	peak early transmitral flow velocity
E_m	=	peak early diastolic myocardial velocity
IVRT	=	isovolumic relaxation time
LA	=	left atrial
LV	=	left ventricular
PV	=	pulmonary vein
S	=	peak systolic pulmonary venous flow
S_m	=	peak systolic myocardial velocity
τ	=	time constant of isovolumic relaxation
TD	=	color M-mode time delay to apical filling
TDE	=	tissue Doppler echocardiography
V_p	=	color M-mode flow propagation velocity

tion time and atrial flow velocity. For instance, in cardiac amyloidosis, progressive elevation in LA pressure causes the Doppler patterns to change from that of delayed relaxation to pseudonormal and finally to restrictive filling with increasing disease severity (21). Since transmitral Doppler filling patterns depend on both parameters, progressive elevation of LA pressure in ventricles with impaired relaxation results in "pseudonormalization" of the filling pattern (1,22).

In an attempt to overcome the limitations of transmitral flow Doppler indices of LV filling, several investigators have incorporated routinely the assessment of PV flow (23–25). With the new generation of ultrasound equipment, direct recordings of PV flow have become almost routinely available from the transthoracic approach. Doppler indices of PV flow have been used in the assessment of LA pressure, differentiation of constrictive pericarditis from restrictive cardiomyopathy and assessment of the severity of mitral regurgitation (26–29). Most normal adult patients exhibit a prominent systolic (S) flow and a systolic-to-diastolic (S/D) ratio >1. In patients with elevated LV filling pressure, reduced LA and LV compliance or with severe mitral regurgitation there is blunting of the pulmonary venous S wave and increased D flow. This pattern, in addition to prominent atrial reversal (AR) flow velocity, has been used to distinguish normal from pseudonormal transmitral Doppler filling (1). However, in normal young adults and athletes in whom atrial contribution to LV filling is minimal and the LA behaves more as a "passive" conduit, blunting of the S wave is also common. Although normal patients may be recognized by their AR velocities of shorter amplitude and duration (30), AR velocities are also frequently diminished in patients with restrictive filling, possibly because of atrial mechanical failure (1,31). In addition, AR amplitude and duration are often difficult to measure in many patients from transthoracic echocardiography.

It is therefore evident that all pulsed Doppler indices of transmitral and PV flow present a parabolic distribution during progression from normal to advanced diastolic dysfunction

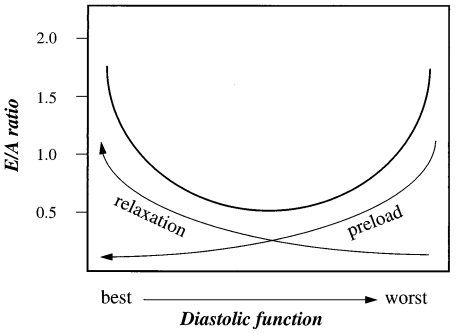

Figure 1. Parabolic curve representing the changes in pulsed Doppler early-to-atrial (E/A) ratio during transition from normal diastolic function to severe dysfunction. Effect of preload and relaxation. Other indices of transmitral and pulmonary venous flow have similar bimodal distribution (see text for details).

(Fig. 1). Determining whether an individual patient is in the left or the right portion of the parabolic curve may be difficult. Careful analysis of Doppler parameters of LV filling and PV flow in combination with two-dimensional echocardiographic and clinical data permits the correct assessment of diastolic function in many patients (32). Nevertheless, in many instances the information obtained from standard pulsed Doppler indices is inconclusive or contradictory. The following part of this presentation will describe how newer indices of LV filling may be used alone or in combination with standard pulsed Doppler to overcome these limitations.

Assessment of LV Filling by Color M-Mode Doppler

While standard pulsed-wave Doppler echocardiography provides the temporal distribution of blood flow velocities in a specific location, color M-mode Doppler echocardiography provides the spatiotemporal distribution of these velocities across a vertical line. Thus the information displayed in a color M-mode recording of the LV inflow is comparable to that given by multiple simultaneous pulse Doppler tracings obtained at different levels from the mitral orifice to the LV apex (Fig. 2).

Physical principles of color M-mode Doppler echocardiography. Color M-mode Doppler displays velocity data along a scanline. Using the autocorrelation method, a series of pairs of ultrasound pulses are sent and their received frequencies are compared. By analyzing the phase shifts, velocities of moving targets are obtained and displayed color encoded. A typical color M-mode Doppler recording provides a temporal resolution of 5 ms, a spatial resolution of about 1 mm and a velocity resolution equal to the forward plus the reversed Nyquist limit divided by 32 (e.g., if both Nyquist limits are 64 cm/s, velocity resolution is 4 cm/s) (33). Figure 3 demonstrates the typical pattern displayed by normal patients in sinus rhythm. A first wave propagates from the LA to the LV apex corresponding to early filling and a second wave follows atrial contraction. The magnitude of these velocities is highest above the mitral leaflet

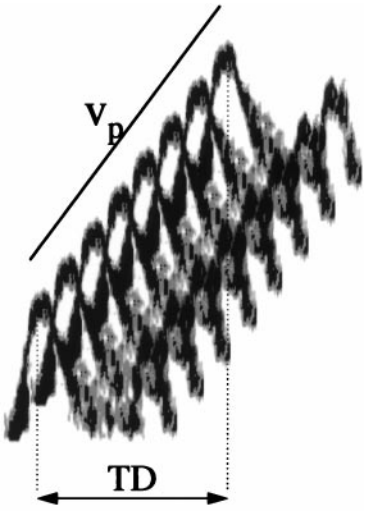

Figure 2. Diagram representing the relationship between pulsed and color M-mode Doppler of the left ventricular inflow. Flow propagation velocity ($\mathbf{V_p}$) is given by the slope of any isovelocity line. Other index reported in the literature is the time delay (**TD**) of the peak E velocity from mitral tips to the apex.

tips and decreases as flow approaches the apex, as shown by the change in encoding color. In normal ventricles, the spatial position of the maximal velocity is closer to the ventricular apex for the early filling (E) wave than it is for the atrial contraction (A) wave, suggesting that intraventricular pressure gradients during early filling produce a suction force that accelerate flow beyond the mitral orifice (34). It is also evident that flow at the mitral valve level occurs earlier than at the apical regions. The velocity at which flow propagates within the ventricle (V_p) is given by the slope of the color wavefront.

Using digital processing, numerical velocity values can be obtained in addition to spatial and temporal information (33). Since color M-mode Doppler provides velocity data simultaneously at multiple spatial locations, in theory it is possible to estimate true pressure gradients using the complete Bernoulli equation (including its inertial term: $p\int_A^V \frac{d\vec{v}}{dt} \cdot d\vec{s}$) (35). If we assume that the direction of the streamlines during LV filling is oriented in parallel with the M-mode cursor line, pressure gradients can be obtained using the Euler equation, a differential form of the Bernoulli equation:

$$-\frac{\partial p}{\partial s}=\rho\left[\frac{\partial v}{\partial t}+v\frac{\partial v}{\partial s}\right].$$

Preliminary data obtained in animals instrumented with multisensor micromanometer catheters at our laboratory have demonstrated that intraventricular pressure gradients calculated by color M-mode Doppler are accurate (36). Intraventricular pressure gradients are thought to be responsible for the mechanism of suction in ventricles with normal relaxation (34). Courtois and Ludbrook (34) have previously shown that these intraventricular gradients result from active myocardial events, suggesting a model of diastolic function that treats the apex as a prominent source of recoil during early diastole, contributing to the process of filling by actively drawing blood from the mid and basal levels of the heart into the apical region. In ischemia and cardiomyopathy these gradients are markedly reduced (37). Studies have shown that in heterogeneous patient populations there is a poor correlation between the propagation velocity (V_p) measured by color M-mode Doppler and pulsed Doppler E velocity (38,39). Vortex formation may explain why flow peak E velocity may be higher than V_p in abnormal ventricles: According to hydrodynamic principles, the velocity of particles (E) in a vortex ring exceeds the velocity at which the whole ring travels (V_p) because of their intrinsic circular motion (40). Vorticity is generated by shear between inflowing blood and the stationary blood already in the ventricle. Contrast studies have shown an increased vortex formation in dilated ventricles and in the presence of apical segmental dysfunction (41).

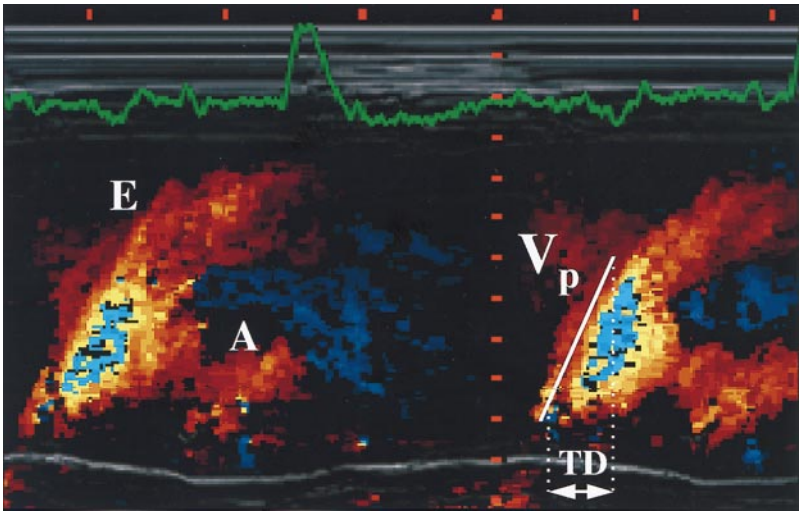

Figure 3. Color M-mode recording of the left ventricular inflow showing the early E and atrial contraction A waves. $\mathbf{V_p}$ = flow propagation velocity; **TD** = time delay (see Figure 2).

Clinical studies using color M-mode Doppler. Several clinical studies have been conducted using either manual or semiautomatic indices derived from color M-mode Doppler. Brun et al. (42) identified the leading edge of the early filling wave (transition from no color-to-color) measured from the mitral leaflet tips to the apex as the flow propagation velocity (V_p). In their study they demonstrated a significant negative correlation between V_p and the time constant of relaxation (τ) in various groups of patients with coronary disease and cardiomyopathy, suggesting that a rapid ventricular relaxation (short τ) promotes a faster propagation of blood into the ventricle. These findings suggested that color M-mode V_p could represent a useful noninvasive index for assessing LV relaxation. Using a different approach, Stuggard et al. (43,44) identified the temporal difference between the point of maximal velocity at the mitral level and at the apex. They demonstrated that this time delay (TD) was prolonged significantly in dogs during ischemia induced by coronary occlusion and in human subjects undergoing coronary angioplasty. Preliminary reports have also shown that TD is reduced by cathecholamine stimulation and prolonged during infusion of beta-antagonists, with changes occurring in parallel with invasive parameters of LV relaxation (43). Recent preliminary clinical studies suggest that color M-mode Doppler may be useful in distinguishing restrictive cardiomyopathy from constrictive pericarditis in patients with preserved systolic function (45). While these patients may have quite similar pulsed-wave Doppler mitral velocity patterns, patients with constrictive pericarditis present an extremely rapid V_p, whereas patients with restrictive cardiomyopathy show distinctly slower V_p than their pulsed E wave velocities. The disparity between pulsed and color M-mode Doppler in patients with restriction could either be caused by abnormal generation of vortices due to functionally reduced mitral valve orifice area and/or by the reduction of intraventricular pressure gradients and thus apical suction force. Further invasive studies will be required to determine the individual contribution of these two factors. Color M-mode Doppler may also be useful to detect diastolic mitral regurgitation frequently found in patients with advanced diastolic dysfunction.

In contrast to standard Doppler filling indices, preliminary experience suggests that V_p is relatively independent of preload. Takatsuji et al. (38) studied a large group of patients with normal, delayed relaxation and pseudonormal pulsed Doppler patterns of LV filling confirmed by hemodynamic findings. While pulsed Doppler indices showed the typical "U shaped" distribution from normal to delayed relaxation to pseudonormal patients, color M-mode Doppler V_p was equally lower in the last two groups. Furthermore, this study also showed a strong negative correlation between τ and V_p, despite the wide variability in LV filling pressures among the three groups of patients.

How to obtain and interpret a color M-mode Doppler study. To record a color M-mode Doppler study the M-mode cursor is placed through the center of the mitral inflow region in the apical four-chamber view. The imaging transducer may be displaced towards the lateral wall if needed to position the M-mode scan line in parallel with the direction of flow observed by two-dimensional color Doppler. The depth is adjusted to include the entire LV from the mitral leaflets to the apex, and the sweep rate is maximized. The V_p may be measured from the still frame on line or recorded on videotape or digital format. The slope that connects any isovelocity line from the tip of the mitral leaflets to the apical regions represents V_p. Careful attention should be made to avoid measuring intracavitary flow originating before the onset of mitral inflow (43). Brun et al. (42) measured originally the slope of the transition from no color-to-color. In our experience we have obtained a higher reproducibility by measuring the slope of the first aliasing velocity from the mitral tips to a position 4 cm distally into the LV (39). This method permits us to obtain a consistent measurement when the color M-mode inflow recordings are curvilinear. The color velocity scale may be adjusted and/or the baseline shifted to produce color aliasing. Recordings should be acquired at end-expiration to minimize misalignment due to translation. Several measurements should be averaged particularly if the patient has an irregular heart rhythm. Color M-mode studies may be difficult to obtain in patients with rapid heart rate and/or first degree atrioventricular block in whom there is poor separation between the early and the atrial filling waves. In our experience, young healthy subjects have a color M-mode $V_p > 55$ cm/s. Older patients or those with LV hypertrophy, normal systolic function and delayed relaxation have lower V_p and low pulsed Doppler E velocity and E/A ratio <1. Patients with advanced diastolic dysfunction have low V_p but higher pulsed Doppler E and E/A >1 (38) (Fig. 4). In some patients with hypertrophic or restrictive cardiomyopathies, intracavitary flow originated before mitral inflow may be very prominent and could be confused with the wave of early filling, giving the appearance of a very fast V_p and should be excluded from measurement.

Tissue Doppler Echocardiography in the Assessment of Diastolic Function

Recently developed for clinical use, tissue Doppler echocardiography (TDE) is a new echocardiographic application that has made possible the acquisition of myocardial velocities on-line during an ultrasound examination (46–48). This technology is now available in several of the new generation ultrasound systems and can provide accurate quantitative information about myocardial motion during the cardiac cycle.

Physical principles of TDE. Doppler ultrasound has been traditionally applied for the measurement of blood flow velocities across intravascular structures. Moving red blood cells reflect low amplitude Doppler signals but at a relatively high velocity. In contrast, moving tissue such as the myocardium typically reflects low velocity but very high amplitude Doppler signals. In a conventional Doppler system a high pass filter is incorporated to eliminate these low velocity signals and the gain settings are increased to amplify the signals reflected by

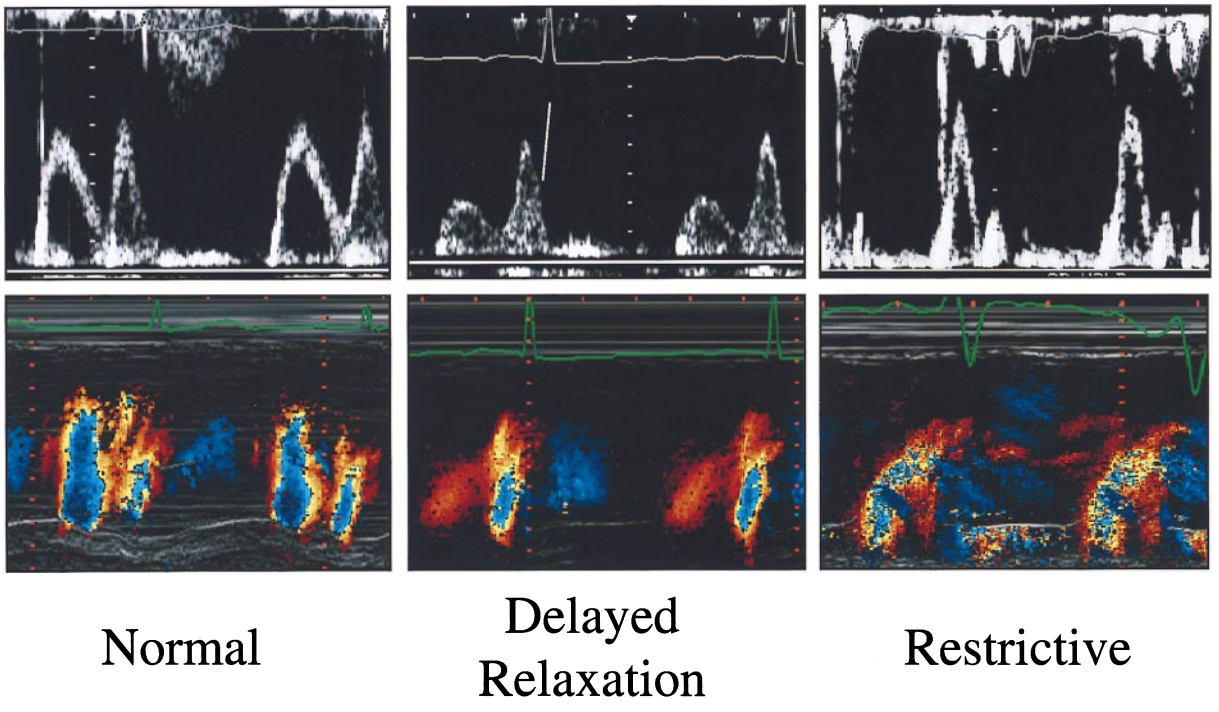

Figure 4. Pulsed and color M-mode Doppler recordings of the left ventricular inflow in a subject with normal diastolic function, a patient with delayed relaxation and a patient with restrictive filling. Notice the delayed apical filling (reduced V_p and prolonged TD in both the delayed relaxation and restrictive cases).

moving blood. To display tissue velocities, two relatively simple alterations in Doppler signal processing are required: 1) the high pass filter is bypassed and 2) a lower gain amplification is used to eliminate the weaker intensity blood flow signals. Tissue Doppler velocities may be displayed either in spectral pulsed or in color-encoded M-mode or two-dimensional mode. The technical principles and limitations of any of these modalities are similar to those encountered with standard Doppler flow systems. The spectral pulsed-wave Doppler method provides the highest temporal and velocity range resolution. The color two-dimensional method provides a high spatial but a low temporal and velocity range resolution (typically 16 velocity values). Tissue Doppler echocardiography may be used to quantify myocardial velocities in multiple segments of the myocardium from different echocardiographic acoustic windows. If we examine a typical spectral display, we can observe a velocity signal directed towards the LV centroid during systole (S_m) and two distinct signals directed away from the centroid during early (E_m) and late (A_m) diastole (Fig. 5). Other multiphasic signals are also frequently detected during isovolumic contraction and relaxation, which are normally not apparent from two-dimensional echocardiography but occasionally can be detected by M-mode (49). These signals are thought to be caused by rapid small geometrical changes that occur in the LV and by right ventricular interdependence (50,51).

To interpret the velocities obtained by either spectral pulsed or color tissue Doppler we must remember that they represent only the component of motion of a given segment in a direction parallel to the imaging cursor. This motion is not only caused by myocardial contraction and relaxation but also by translation and rotation of the cardiac structures. Several algorithms have been proposed to eliminate the effect of translation and to correct for Doppler angle misalignment. A different approach that we and other investigators have used measures the axial motion of the ventricle by interrogating the basal myocardial segment near the mitral annular region from the apical acoustic window (52,53). Since the position of the apex is relatively fixed throughout the cardiac cycle and the motion of the base in the axial plane is near in parallel with the Doppler cursor, the velocities obtained almost entirely represent the motion due to contraction and relaxation and do not require angle correction. Regional LV systolic and diastolic function can be assessed by placing the sample volume at different segments of the septal, lateral, anterior, inferior and posterior myocardial walls from the two-, three- and four-chamber apical views. Global function may be expressed as the average of these regions, particularly in those patients with regional wall motion abnormalities.

Clinical studies using TDE. In healthy normal subjects, the motion of the myocardium during diastole in either the circumferential or the axial plane appears as a mirror image of the mitral inflow velocity patterns. A fall in the ratio of the myocardial E_m velocity to A_m velocity with age is noted, as it has been previously well described in the LV filling curves. However, the concordance observed between diastolic myocardial velocities in the axial plane and ventricular inflow patterns is disrupted in various disease states. In patients with restrictive

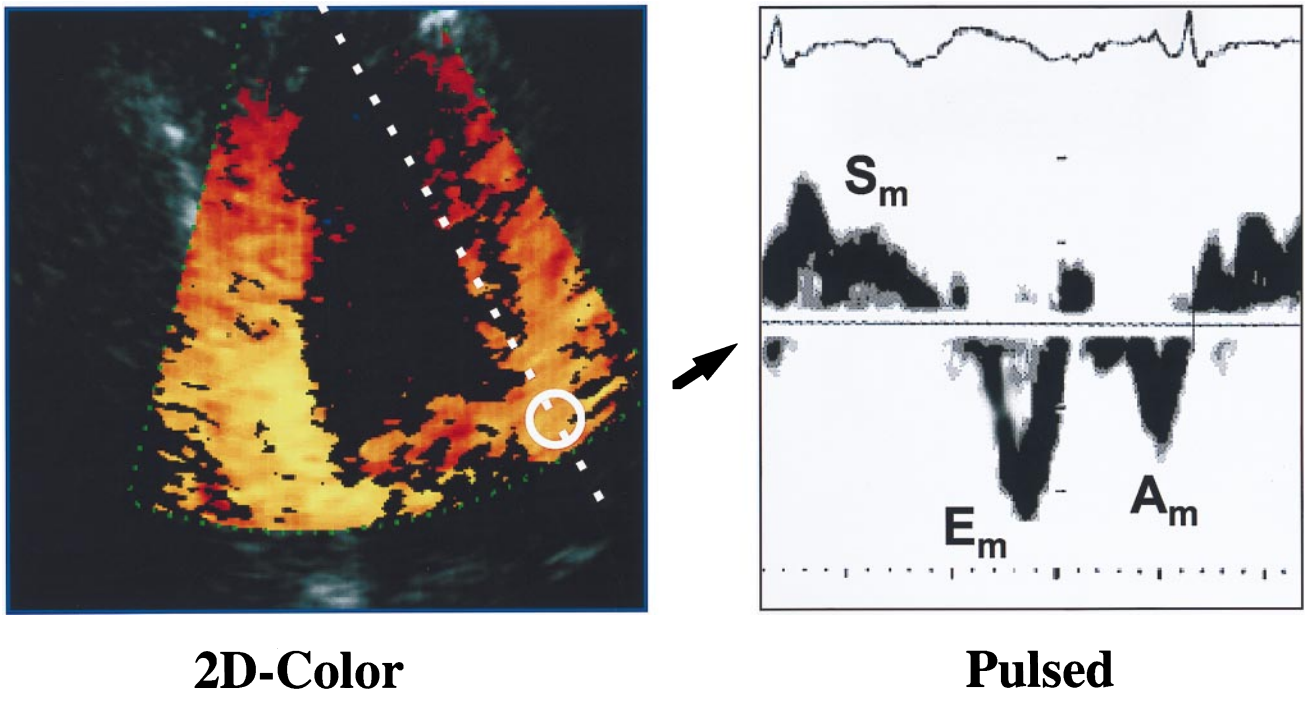

Figure 5. Two-dimensional color and pulsed tissue Doppler axial velocities of the myocardium recorded from the apical four-chamber view. Systolic (S_m), early diastolic (E_m) and atrial contraction (A_m) velocities are shown in the pulsed Doppler tracing. The two-dimensional image was obtained during systole.

cardiomyopathy we have found low E_m in the presence of either low or high pulsed Doppler E velocities and frequently a E_m/A_m ratio <1 in patients with pseudonormalized or restrictive filling (E/A ratio >1) (54) (Fig. 6). Based on this observation we have used TDE to differentiate restrictive cardiomyopathy from constrictive pericarditis. In contrast to patients with restriction, patients with pure constrictive pericarditis and normal systolic function have normal or even elevated E_m velocities, probably indicating normal ventricular relaxation. In this preliminary study we found that a cutoff pulsed Doppler E_m velocity of 8 cm/s allowed complete separation between patients with constriction and restriction (Fig. 7). These results have been recently confirmed in a larger, prospective cohort (54). Similar discordance between LV filling ratios and myocardial velocities may be found in patients with hypertrophic, dilated and hypertensive cardiomyopathies (55,56). Myocardial diastolic velocities have been reported to differentiate myocardial hypertrophy in athletes from hypertrophic cardiomyopathy with an accuracy of >0.9 (57). In this study no significant difference was found in standard Doppler indices of LV filling among these two groups. These observations have suggested that changes in E_m velocity caused by impaired LV relaxation are less sensitive to preload compensation. Oki et al. (58) recorded transmitral flow and myocardial Doppler velocities and measured τ in patients undergoing cardiac catheterization. The time constant (τ) correlated well with IVRT and other various parameters calculated from transmitral flow Doppler, except in those patients with elevated LV end-diastolic pressure who presented a pseudonormal filling pattern. In contrast, all patients with heart disease who had abnormal LV relaxation (prolonged τ) also had a low E_m. Moreover, τ correlated well with E_m in all subjects, regardless of their LV filling pressure. In a recent study, Sohn and coworkers (56) measured myocardial velocities in normal volunteers and in patients with delayed relaxation and pseudonormal LV filling as assessed by Doppler mitral inflow variables and invasive hemodynamic measurements. In patients with a mitral Doppler inflow pattern of delayed relaxation, the infusion of volume resulted in a change towards pseudonormalization with shortening of the E wave deceleration time and increased E/A ratio, while patients with normal or pseudonormal filling at baseline demonstrated a significant reduction in mitral inflow E velocity and E/A ratio after nitroglycerin infusion. In contrast, no significant changes were found in E_m velocity, confirming that this parameter is less sensitive to preload changes. In this study, patients with pseudonormal filling, defined as the combination of normal mitral inflow variables and prolonged τ (> or = 50 ms) could be separated from patients with normal filling patterns by an E_m velocity <8.5 cm/s and a E_m/A_m ratio <1 with a sensitivity of 88% and specificity of 67%. A similar study conducted in our laboratory including patients with various degrees of diastolic dysfunction recently showed that E_m was the best discriminator between normal and pseudonormal patients when compared to any other single or combined index of transmitral filling and pulmonary venous Doppler flows (59). Doppler myocardial E_m velocity is remarkably low in patients with hypertrophic or restrictive cardiomyopathies with either delayed relaxation,

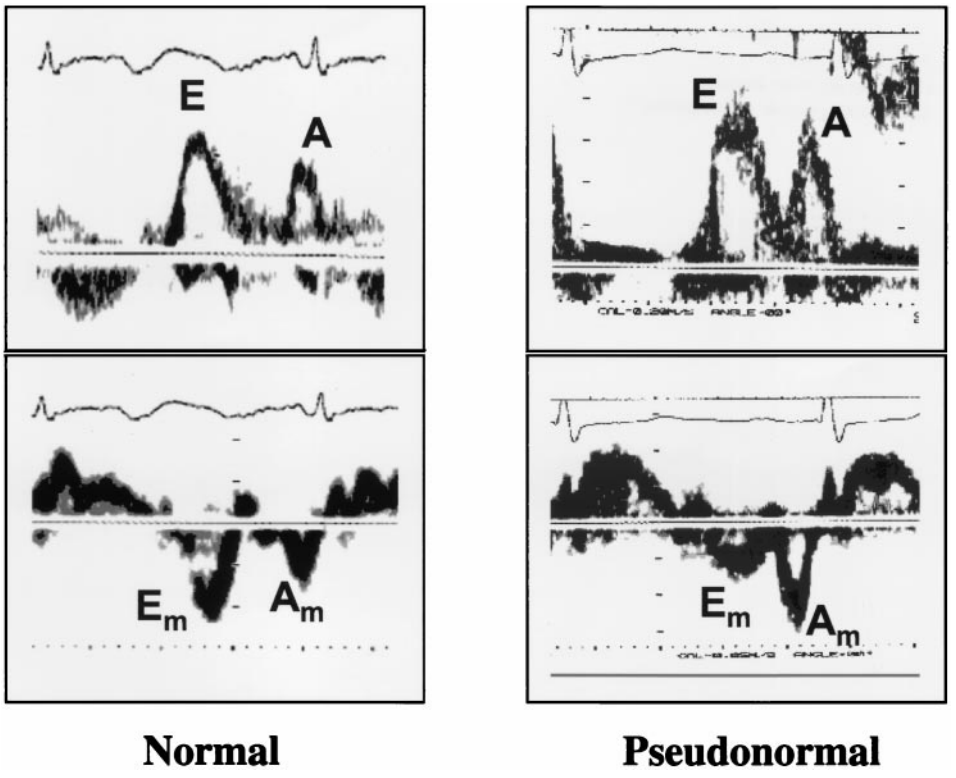

Figure 6. Standard pulsed Doppler transmitral inflow (**upper panels**) and myocardial axial velocities (**lower panels**) recorded at the basal lateral wall in a healthy volunteer and in a patient with severe aortic stenosis, left ventricular hypertrophy and elevated filling pressures (pseudonormal). Early diastolic myocardial velocity (E_m) is significantly reduced as well as the early-to-atrial velocity ratio (E_m/A_m) in the pseudonormal patient (see text for details).

pseudonormal or restrictive filling, even in the presence of preserved systolic function (60). Preliminary data suggest that diastolic myocardial velocities measured by TDE are very sensitive in detecting rejection in heart transplant patients (60).

How to obtain and interpret a TDE study. We as well as other investigators have proposed to measure myocardial velocities in the longitudinal axis to minimize the effect of cardiac translation (54,56,57,59). From either the apical four-chamber or two-chamber acoustic windows, the region of

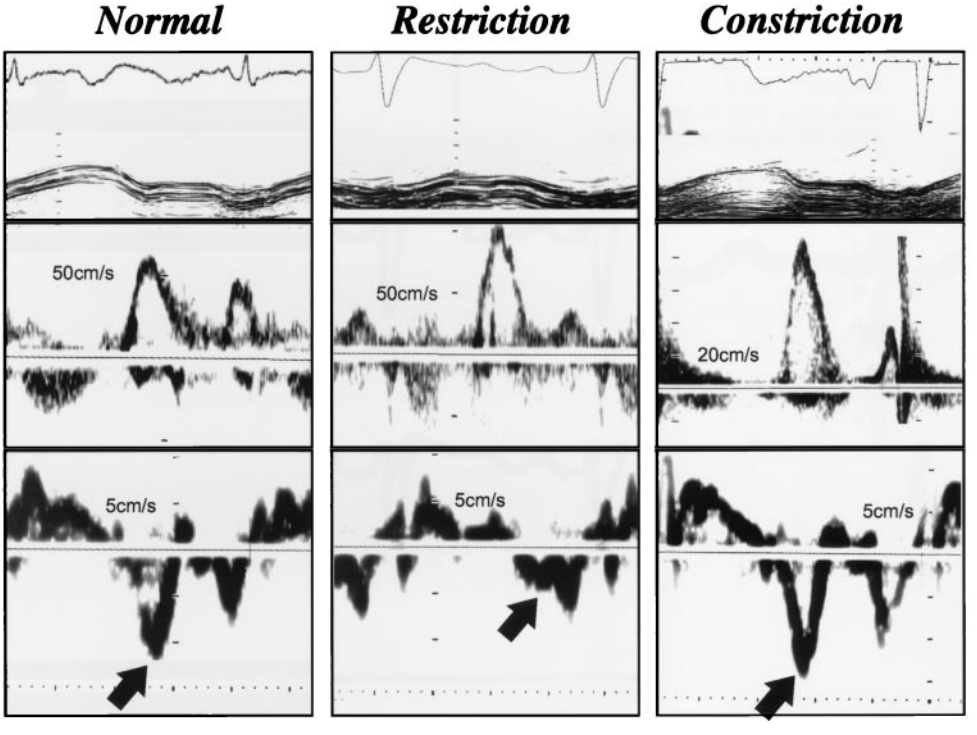

Figure 7. Differentiation of restrictive cardiomyopathy from constrictive pericarditis. Representative examples of the mitral annular M-mode, tissue Doppler axial velocities and transmitral Doppler flow velocities in a normal volunteer, a patient with restrictive cardiomyopathy and a patient with constrictive pericarditis. A marked difference in early diastolic velocity (**arrows**) despite similar transmitral flow velocities is appreciated.

Table 1. Stages of Diastolic Dysfunction (see text for details)

	Normal (young)	Normal (adult)	Delayed Relaxation	Pseudonormal Filling	Restrictive Filling
E/A (cm/s)	>1	>1	<1	1–2	>2
DT (ms)	<220	<220	>220	150–200	<150
IVRT (ms)	<100	<100	>100	60–100	<60
S/D	<1	≥1	≥1	<1	<1
AR (cm/s)	<35	<35	<35	≥35*	≥25*
V_p (cm/s)	>55	>45	<45	<45	<45
E_m (cm/s)	>10	>8	<8	<8	<8

*Unless atrial mechanical failure is present. AR = pulmonary venous peak atrial contraction reversed velocity; DT = early left ventricular filling deceleration time; E/A = early-to-atrial left ventricular filling ratio; E_m = peak early diastolic myocardial velocity; IVRT = isovolumic relaxation time; S/D = systolic-to-diastolic pulmonary venous flow ratio; V_p = color M-mode flow propagation velocity.

interest is placed at the level of mitral annulus either on the septal, lateral, anterior or posterior aspects. Two-dimensional or color M-mode recordings must be analyzed on line or recorded digitally to decode the color-encoded velocity values. Spectral pulsed Doppler studies may be recorded in videotape. Studies are obtained during apnea to minimize translation-induced motion artifacts. Color or pulsed Doppler gains are minimized and the wall filter is eliminated. Peak early diastolic velocity is measured at the time of the electrocardiographic T wave. Peak atrial contraction velocity is the next major deflection following the electrocardiographic A wave. The magnitude of these velocities may vary according to the location, particularly if the patient has regional wall motion abnormalities. In these cases an estimate of global performance could be derived by averaging velocities obtained from different myocardial segments. In normal subjects E_m and E_m/A_m ratio decrease with age in a similar manner to pulsed E and E/A of the transmitral flow (56). Older patients or those with LV hypertrophy, normal systolic function and delayed relaxation have lower V_p and low pulsed Doppler E velocity and E/A ratio <1 (38). Because of their relative preload independence, diastolic myocardial velocities may be used to differentiate normal from pseudonormal filling patterns. Patients with advanced diastolic dysfunction and pseudonormal filling have lower E_m compared to those with normal filling (57).

Incorporating Color M-Mode and Tissue Doppler Indices Into the Conventional Stages of Diastolic Function

The general clinical and echocardiographic evaluation of diastolic function recognizes four distinct stages from normal to advanced disease. Table 1 incorporates color M-mode and tissue Doppler parameters to the criteria accepted by the Canadian Consensus on Diastolic Dysfunction (61). These patterns are not unique to a specific disease but represent a spectrum, which may be influenced by aging and changing hemodynamic variables.

Normal filling pattern. The normal filling pattern is seen in patients with normal LV relaxation rate, compliance and filling pressures. Atrial contribution to LV filling is minimal. Thus, standard Doppler indices of LV filling and PV flow are characterized by high E, E/A ratio <1, IVRT <100 ms and early filling deceleration time (DT) <220 ms. In young adults, athletes and pregnancy the very rapid relaxation rate results in rapid and near-complete LV filling during early diastole, causing very short IVRT, prominent E and short DT. The LA behaves primarily as a reservoir and conduit. Since LA volume before atrial contraction is minimal, LA contractility is reduced, resulting in low ejection volume, A and AR velocities, reduced LA relaxation force and consequently low S. As atrial contribution to LV filling increases with age, A and S become more prominent and S/D ratio becomes >1. Color M-mode V_p is fast, in our experience >55 cm/s in younger and >45 cm/s in older adults. Tissue Doppler echocardiography E_m velocity measured in the LV long axis plane is >10 and >8 cm/s, respectively.

Stage I (delayed relaxation). This pattern is seen in patients with reduced LV relaxation rate but relatively normal compliance and filling pressures. Patients typically have only mild symptoms or are asymptomatic and may have mild LA enlargement. Atrial contribution to LV filling is increased, frequently >30% of the stroke volume. The delayed relaxation pattern is characterized by an E/A ratio <1, prolonged DT (>220 ms) and IVRT (>100 ms). Pulmonary venous flows show S > D with usually prominent AR. Color M-mode V_p is reduced (<45 cm/s), as well as TDE E_m (<8 cm/s).

Stage II (pseudonormal). This pattern is often the most difficult to recognize since, as its name implies, Doppler filling indices resemble those found in normal subjects. Left ventricular relaxation rate and compliance are reduced, but filling pressure is now increased as a compensatory or overcompensatory mechanism to maintain cardiac output. Patients have mild-to-moderate symptoms of pulmonary vascular congestion and various degrees of LA enlargement depending upon the chronicity of disease. Other evidence of structural heart disease, such as increased LV volumes and mass and reduced ejection fraction, is also commonly present. The elevated LA pressure results in earlier opening of the mitral valve and, thus, shorter IVRT. The reduced LV compliance causes rapid increase in LV pressure with cessation of LV filling and reduced DT. Atrial contribution to LV filling is reduced due to the increased end-diastolic LV stiffness resulting in reduced A and pulmonary venous S/D <1. Pulmonary venous AR is >35 cm/s unless atrial mechanical failure is present. Since LV relaxation is impaired, color M-mode V_p remains reduced, <45 cm/s, as well as TDE E_m (<8 cm/s).

Stage III (restrictive filling). The last clinical filling pattern is seen in the presence of profound abnormalities of LV compliance and markedly increased filling pressure. Left ventricular relaxation is reduced, perhaps with the only exception being patients with isolated constrictive pericarditis. Patients have overt heart failure and moderate-to-severe LA enlargement depending upon the chronicity of disease. Echocardio-

graphic features of advanced structural heart disease are evident by now. Standard Doppler filling indices are characterized by an increased E/A ratio (>2), short DT (<150 ms) and IVRT (<60 ms). Pulmonary venous flow usually shows markedly blunted S. Prominent AR is frequently not present, probably because of atrial mechanical failure, and usually carries a poor prognosis (62). Color M-mode V_p and TDE E_m are the lowest, except in patients with constrictive pericarditis in whom LV relaxation is normal.

Estimation of LV Filling Pressure

Standard Doppler indices of LV filling and PV flow have been used to estimate noninvasively LV filling pressure (63–66). All these previously proposed methods are accurate when applied to groups of patients with homogeneously impaired LV relaxation, since they assume that reduction in IVRT, atrial filling fraction, PV S/D ratio and DT will occur solely as a consequence of elevated LA pressure. However, when these methods are applied to younger patients and those with minimal structural heart disease (65,67), they overestimate actual LV filling pressure, since they cannot separate the effect of LV relaxation and preload as confounding variables. Color M-mode and tissue Doppler velocities used as an index of LV relaxation may be combined with standard Doppler flow indices to separate these confounding effects. As previously discussed, LA pressure and LV relaxation are the main determinants of pulsed Doppler E velocity. A positive linear relation between E and LA pressure and a negative but still linear inverse relationship between E and τ have been shown in animal experiments. Since there is a strong (negative) linear correlation between V_p and τ, we can combine pulsed and color M-mode Doppler data to predict LA pressure ($LAP = 5.27*(E/V_p) + 4.6$ mm Hg, $r = 0.80$, $p < 0.001$, SEE = 3.1 mm Hg) (39). This equation not only has been developed and validated in relatively heterogeneous groups of patients admitted to the coronary, medical and surgical intensive care units, but it is also theoretically and intuitively sound. A normal subject with rapid relaxation under normal preload conditions will have both increased E and V_p. A subject with impaired relaxation and normal preload will have both reduced E and V_p. In contrast, a patient with impaired relaxation but elevated preload will exhibit a prominent E but a reduced V_p. In a recent study, the combination of standard pulsed Doppler and diastolic myocardial velocities measured by TDE seemed also to provide an accurate estimation of LV filling pressure (68).

Limitations

Further studies will be required to address the limitations of these new Doppler applications. Although preliminary data suggest that these two methods are relatively preload independent, the effect of varying preload conditions, heart rate and atrioventricular conduction on these variables remains to be rigorously tested.

The measurement of color M-mode Doppler needs to be standardized. The impact of variable transducer and pulse repetition frequencies needs to be studied to determine whether the suggested range of normal values is comparable among different ultrasound systems. Automated algorithms are being developed to facilitate these measurements.

The major limitation of TDE measurements is their angle dependency. Although several algorithms, such as the measurement of myocardial velocity gradients, have been suggested to correct for the Doppler beam angle of incidence, the application of this technique is still limited to interrogating a limited number of myocardial segments from the different acoustic windows. It has been particularly problematic to study the apical myocardial segments with this technique.

The agreement between pulsed and color tissue Doppler-derived velocities has not been systematically studied. Based in ranges of normal values published in the literature, it appears that pulsed Doppler-derived velocities are higher. This difference may be attributed to greater spatiotemporal smoothing with the color technique or to differences by measuring peak velocities using the edge of the spectral pulsed Doppler envelope vs. mean velocities by color Doppler.

The relative information obtained from tissue Doppler velocities and by color M-mode Doppler assessment of LV filling needs to be compared in future studies. Disparities between these two techniques could occur in some patients, particularly in those with segmental wall motion abnormalities since color M-mode Doppler provides a global assessment of diastolic function, while TDE provides regional information.

Conclusions. Newer applications in echocardiography are revolutionizing the study of patients with diastolic dysfunction. These applications appear to have finally overcome the limitations of standard Doppler techniques separating the effects of preload and relaxation in LV filling. Further studies will be needed in the future to standardize and develop automated measuring methods and to establish ranges of values from larger patient populations. The clinical diagnostic and prognostic utility derived from these will likely be shown during the next decade after they are routinely incorporated into the echocardiographic evaluation of diastolic function.

References

1. Appleton CP, Hatle L, Popp RL. Relation of transmitral flow velocity patterns to left ventricular diastolic function: new insights from a combined hemodynamic and Doppler echocardiographic study. J Am Coll Cardiol 1988;12:426–40.
2. Hoit BD, Walsh RA. Diastolic function in hypertensive heart disease. In: Gaasch WH, LeWinter M, editors. Left Ventricular Diastolic Dysfunction and Heart Failure. Philadelphia: Lea and Febiger, 1994:354–72.
3. Labovitz AJ, Pearson AC. Evaluation of left ventricular diastolic function: clinical relevance and recent Doppler echocardiographic insights. Am Heart J 1987;114:836–51.
4. Nishimura RA, Abel MD, Hatle LK, Tajik AJ. Assessment of diastolic function of the heart: background and current applications of Doppler echocardiography. Part II: clinical studies. Mayo Clin Proc 1989;64:181–204.
5. Pinamonti B, Zecchin M, Di Lenarda A, Gregori D, Sinagra G, Camerini F. Persistence of restrictive left ventricular filling pattern in dilated cardiomyopathy: an ominous prognostic sign. J Am Coll Cardiol 1997;29:604–12.
6. Giannuzzi P, Temporelli PL, Bosimini E, et al. Independent and incremental prognostic value of Doppler-derived mitral deceleration time of early filling

in both symptomatic and asymptomatic patients with left ventricular dysfunction. J Am Coll Cardiol 1996;28:383–90.
7. Rihal CS, Nishimura RA, Hatle LK, Bailey KR, Tajik AJ. Systolic and diastolic dysfunction in patients with clinical diagnosis of dilated cardiomyopathy. Relation to symptoms and prognosis. Circulation 1994;90:2772–9.
8. Pinamonti B, Di Lenarda A, Sinagra G, Camerini F. Restrictive left ventricular filling pattern in dilated cardiomyopathy assessed by Doppler echocardiography: clinical, echocardiographic and hemodynamic correlations and prognostic implications. J Am Coll Cardiol 1993;22:808–15.
9. Lahiri A, Rodrigues EA, Carboni GP, Raftery EB. Effects of long-term treatment with calcium antagonists on left ventricular diastolic function in stable angina and heart failure. Circulation 1990;81 Suppl III:130–8.
10. Appleton CP, Hatle LK. The natural history of left ventricular filling abnormalities: assessment by two-dimensional and Doppler echocardiography. Echocardiography 1992;9:437–45.
11. Choong CY, Abascal VM, Thomas JD, Guerrero JL, McGlew S, Weyman AE. Combined influence of ventricular loading and relaxation on the transmitral flow velocity profile in dogs measured by Doppler echocardiography. Circulation 1988;78:672–83.
12. Colan SD, Borow KM, Neumann A. Effects of loading conditions and contractile state (methoxamine and dobutamine) on left ventricular early diastolic function in normal subjects. Am J Cardiol 1985;55:790–6.
13. Ishida Y, Meisner JS, Tsujioka K, et al. Left ventricular filling dynamics: influence of left ventricular relaxation and left atrial pressure. Circulation 1986;74:187–96.
14. Thomas JD, Weyman AE. A fluid dynamics model of mitral valve flow: description with in vitro validation. J Am Coll Cardiol 1989;13:221–33.
15. Thomas JD, Weyman AE. Echo-Doppler evaluation of left ventricular diastolic function: physics and physiology. Circulation 1991;84:977–99.
16. Flachskampf FA, Rodriguez LL, Chen C, Guerrero JL, Weyman AE, Thomas JD. Analysis of mitral inertance: a factor critical for early transmitral filling. J Am Soc Echocardiogr 1993;6:422–32.
17. Vandervoort PM, Greenberg NL, Thomas JD. Relative importance of convective and inertial forces during left ventricular filling (abstr). J Am Coll Cardiol 1995;25:335A.
18. Bryg RJ, Pearson AC, Williams GA, Labovitz AJ. Left ventricular systolic and diastolic flow abnormalities determined by Doppler echocardiography in obstructive hypertrophic cardiomyopathy. Am J Cardiol 1987;59:925–31.
19. Bryg RJ, Williams A, Labovitz AJ. Effect of aging on left ventricular diastolic filling in normal subjects. Am J Cardiol 1987;59:971–4.
20. Maron BJ, Spirito P, Green KJ, Wesley YE, Bonow RO, Arce J. Noninvasive assessment of left ventricular diastolic function by pulsed Doppler echocardiography in patients with hypertrophic cardiomyopathy. J Am Coll Cardiol 1987;10:733–42.
21. Klein AL, Hatle LK, Burstow D, et al. Doppler characterization of left ventricular diastolic function in cardiac amyloidosis. J Am Coll Cardiol 1989;13:1017-26.
22. Little WC, Ohno M, Kitzman DW, Thomas JD, Cheng CP. Determination of left ventricular chamber stiffness from the time for deceleration of early left ventricular filling. Circulation 1995;92:1933–9.
23. Keren G, Meisner JS, Sherez J, Yellin EL, Laniado S. Interrelationship of mid-diastolic mitral valve motion, pulmonary venous flow, and transmitral flow. Circulation 1986;74:36–44.
24. Basnight MA, Gonzalez MS, Kershenovich SC, Appleton CP. Pulmonary venous flow velocity: relation to hemodynamics, mitral flow velocity and left atrial volume, and ejection fraction. J Am Soc Echocardiogr 1991;4:547–58.
25. Masuyama T, Jung-Myung L, Yamamoto K, Tanouchi J, Hori M, Kamada T. Analysis of pulmonary venous flow velocity patterns in hypertensive hearts: its complementary value in the interpretation of mitral flow velocity patterns. Am Heart J 1992;124:983–94.
26. Appleton CP, Gonzalez MS, Basnight MA. Relationship of left atrial pressure and pulmonary venous flow velocities: importance of baseline mitral and pulmonary venous flow patterns studied in lightly sedated dogs. J Am Soc Echocardiogr 1994;7:264–75.
27. Nakatani S, Yoshitomi H, Wada K, Beppu S, Nagata S, Miyatake K. Noninvasive estimation of left ventricular end-diastolic pressure using transthoracic Doppler-determined pulmonary venous atrial flow reversal. Am J Cardiol 1994;73:1017–8.
28. Schiavone WA, Calafiore PA, Salcedo EE. Transesophageal Doppler echocardiographic demonstration of pulmonary venous flow velocity in restrictive cardiomyopathy and constrictive pericarditis. Am J Cardiol 1989;63:1286–8.
29. Castello R, Pearson A, Lenzen P, Labovitz AJ. Effect of mitral regurgitation on pulmonary venous velocities derived from transesophageal echocardiography color guided pulsed Doppler imaging. J Am Coll Cardiol 1991;17:1499–506.
30. Rossvoll O, Hatle LK. Pulmonary venous flow velocities recorded by transthoracic Doppler ultrasound: relation to left ventricular diastolic pressures. J Am Coll Cardiol 1993;21:1687–96.
31. Plehn JF, Southworth J, Cornwell GG III. Brief report: atrial systolic failure in primary amyloidosis. N Engl J Med 1992;327:1570–3.
32. Nishimura RA, Tajik AJ. Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography is the clinician's Rosetta stone. J Am Coll Cardiol 1997;30:8–18.
33. Thomas JD, Vandervoort PM, Greenberg NL, Ares MA, Adams MS. Application of color Doppler M-mode echocardiography in the assessment of ventricular diastolic function: analysis of the spatiotemporal velocity distribution. In: Ingels NB Jr, Daughters GT, Baan J, Covell JW, Reneman RS, Yin F C-P, editors. Systolic and Diastolic Function of the Heart. Amsterdam: IOS Press, 1996;101–18.
34. Courtois M, Ludbrook PA. Intraventricular pressure transients during relaxation and filling. In: Gaasch WH, LeWinter MM, editors. Left Ventricular Diastolic Dysfunction and Heart Failure. Philadelphia: Lea & Febiger, 1994:150–66.
35. Greenberg NL, Vandervoort PM, Thomas JD. Instantaneous diastolic transmitral pressure differences from color Doppler M Mode echocardiography. Am J Physiol 1996;271:H1267–76.
36. Greenberg NL, Vandervoort PM, Thomas JD. Estimation of diastolic intraventricular pressure gradients from color Doppler M-mode spatiotemporal velocities: analytical Euler equation solution. Los Alamitos, CA: Computers in Cardiology 1994, IEEE Computer Society Press, 1995:465–8.
37. Ling D, Rankin JS, Edwards CH, McHale PA, Anderson RW. Regional diastolic mechanics of the left ventricle in the conscious dog. Am J Physiol 1979;236:H323–30.
38. Takatsuji H, Mikami T, Urasawa K, et al. A new approach for evaluation of left ventricular diastolic function: spatial and temporal analysis of left ventricular filling flow propagation by color M-mode Doppler echocardiography. J Am Coll Cardiol 1996;27:365–71.
39. Garcia MJ, Ares MA, Asher C, Rodriguez L, Vandervoort P, Thomas JD. Color M-mode flow velocity propagation: an index of early left ventricular filling that combined with pulsed Doppler peak E velocity may predict capillary wedge pressure. J Am Coll Cardiol 1997;29:448–54.
40. Steen T, Steen S. Filling of a model left ventricle studied by colour M mode Doppler. Cardiovasc Res 1994;28:1821–27.
41. Beppu S, Izumi S, Miyatake K, et al. Abnormal blood pathways in left ventricular cavity in acute myocardial infarction. Experimental observations with special reference regional wall motion abnormality and hemostasis. Circulation 1988;78:157–64.
42. Brun P, Tribouilloy C, Duval AM, et al. Left ventricular flow propagation during early filling is related to wall relaxation: a color M-mode Doppler analysis. J Am Coll Cardiol 1992;20:420–32.
43. Stugaard M, Risoe C, Ihlen H, Smiseth OA. Intracavitary filling pattern in the failing left ventricle assessed by color M-mode Doppler echocardiography. J Am Coll Cardiol 1994;24:663–70.
44. Stugaard M, Smiseth OA, Risoe C, Ihlen H. Intraventricular early diastolic filling during acute myocardial ischemia: assessment by multigated color M-mode Doppler echocardiography. Circulation 1993;88:2705–13.
45. Rodriguez L, Ares MA, Vandervoort PM, Thomas JD, Greenberg N, Klein A. Does color M-mode flow propagation differentiate between patients with restrictive vs. constrictive physiology? (abstr). J Am Coll Cardiol 1996;27:268A.
46. McDiken WN, Sutherland GR, Moran CM, Gordon LN. Colour Doppler velocity imaging of the myocardium. Ultrasound Med Biol 1992;18:651–4.
47. Isaaz K, Thompson A, Ethevenot G, Cloez JL, Brembilla B, Pernot C. Doppler echocardiographic measurement of low velocity motion of the left ventricular posterior wall. Am J Cardiol 1989;64:66–75.
48. Miyatake K, Yamagishi M, Tanaka N, et al. New method for evaluating left ventricular wall motion by color-coded tissue Doppler imaging: in vitro and in vivo studies. J Am Coll Cardiol 1995;25:717–24.
49. Garcia MJ, Rodriguez L, Ares M, et al. Myocardial wall velocity assessment by pulsed Doppler tissue imaging: characteristic findings in normal subjects. Am Heart J 1996;132:648–56.
50. Gibson DG, Doran JH, Traill TA, Brown DJ. Abnormal left ventricular wall movement during early systole in patients with angina pectoris. Br Heart J 1984;51:70–6.

51. Gibson DG, Prewitt TA, Brown DJ. Analysis of left ventricular wall movement during isovolumic relaxation and its relation to coronary artery disease. Br Heart J 1976;38:1010–9.
52. Isaaz K, Munoz del Romeral L, Lee E, Schiller NB. Quantitation of the motion of the cardiac base in normal subjects by Doppler echocardiography. J Am Soc Echocardiogr 1993;6:166–76.
53. Garcia MJ, Rodriguez L, Ares MA, Griffin BP, Thomas JD, Klein AL. Differentiation of constrictive pericarditis from restrictive cardiomyopathy: assessment of left ventricular diastolic velocities in the longitudinal axis by Doppler tissue imaging. J Am Coll Cardiol 1996;27:108–14.
54. Rajagopalan N, Garcia MJ, Rodriguez L, Murray RD, Klein AL. Comparison of Doppler echocardiographic methods to differentiate constrictive pericarditis from restrictive cardiomyopathy. J Am Coll Cardiol 1998;31:164A.
55. Rodriguez L, Garcia MJ, Ares MA, Griffin BP, Nakatani S, Thomas JD. Assessment of mitral annular dynamics during diastole by Doppler tissue imaging: comparison with mitral Doppler inflow in subjects without heart disease and in patients with left ventricular hypertrophy. Am Heart J 1996;131:982–7.
56. Sohn DW, Chai IH, Lee DJ, et al. Assessment of mitral annulus velocity by Doppler tissue imaging in the evaluation of left ventricular diastolic function. J Am Coll Cardiol 1997;30:474–80.
57. Palka P, Lange A, Fleming AD, et al. Differences in myocardial velocity gradient measured throughout the cardiac cycle in patient with hypertrophic cardiomyopathy, athletes and patients with left ventricular hypertrophy due to hypertension. J Am Coll Cardiol 1997;30:760–8.
58. Oki T, Tabata T, Yamada H, et al. Clinical application of pulsed Doppler tissue imaging for assessing abnormal left ventricular relaxation. Am J Cardiol 1997;79:921–8.
59. Farias CA, Rodriguez L, Sun JP, Garcia MJ, Klein AL, Thomas JD. Assessment of diastolic dysfunction by conventional Doppler and Doppler tissue imaging (abstr). Circulation 1997;96:I-343.
60. Mankad S, Murali S, Mandarino WA, Kormos RL, Gorcsan J III. Assessment of acute cardiac allograft rejection by quantitative tissue Doppler echocardiography. Circulation 1997;96:I-342.
61. Rakowski H, Appleton C, Chan KL, et al. Canadian consensus recommendations for the measurement and reporting of diastolic dysfunction by echocardiography: from the investigators of Consensus on Diastolic Dysfunction by Echocardiography (review). J Am Soc Echocardiogr 1996;9:736–60.
62. Klein AL, Hatle LK, Taliercio CP, Oh JK, et al. Prognostic significance of Doppler measures of diastolic function in cardiac amyloidosis. A Doppler echocardiography study. Circulation 1991;83:808–16.
63. Vanoverschelde JL, Raphael DA, Robert AR, Cosyns JR. Left ventricular filling in dilated cardiomyopathy: relation to functional class and hemodynamics. J Am Coll Cardiol 1990;15:1288–95.
64. Stork TV, Muller RM, Piske GJ, Ewert CO, Hochrein H. Noninvasive measurement of left ventricular filling pressures by means of transmitral pulsed Doppler ultrasound. Am J Cardiol 1989;64:655–60.
65. Mulvagh S, Quinones MA, Kleiman NS, Cheirif J, Zoghbi WA. Estimation of left ventricular end-diastolic pressure from Doppler transmitral flow velocity in cardiac patients independent of systolic performance. J Am Coll Cardiol 1992;20:112–9.
66. Vanoverschelde JL, Robert AR, Gerbaux A, Michel X, Hanet C, Wijns W. Noninvasive estimation of pulmonary arterial wedge pressure with Doppler transmitral flow velocity pattern in patients with known heart disease. Am J Cardiol 1995;75:383–9.
67. Nagueh SF, Kopelen HA, Zoghbi WA. Feasibility and accuracy of Doppler echocardiographic estimation of pulmonary artery occlusive pressure in the intensive care unit. Am J Cardiol 1995;75:1256–62.
68. Nagueh SF, Middleton KJ, Kopelen HA, Zoghbi WA, Quinones MA. Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. J Am Coll Cardiol 1997;30:1527–33.